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Licata & Tyrrell P.C. 66 East Main Street Marlton, NJ 08053				SPIEGLER, ALEXANDER H
		ART UNIT	PAPER NUMBER	1637

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/016,349	RECIPON ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 03 May 2004.

2a) This action is **FINAL**.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-5,7-9,15 and 18-28 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-5, 7-9, 15 and 18-28 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

)  Notice of References Cited (PTO-892)      4)  Interview Summary (PTO-413)  
 )  Notice of Draftsperson's Patent Drawing Review (PTO-948)      Paper No(s)/Mail Date. \_\_\_\_\_.  
 )  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_.      5)  Notice of Informal Patent Application (PTO-152)  
 )  Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Status of the Application***

1. This action is in response Applicants' response, filed on May 3, 2004. Claims 1-5, 7-9, 15 and 18-28 are pending and have been rejected herein. This action contains new rejections necessitated by Applicants' amendments. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

### **THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS**

#### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-5, 7-9, 15 and 18-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-5, 7-9, 15 and 18-28 are indefinite over "lung cancer specific" because it is not clear as to whether this nucleic acid (either RNA or DNA) is only found in lung cancer samples, is expressed only in lung cancer samples, or could be found or expressed in other samples, such as samples that are not lung cancer samples (e.g., testes). In addition, since all cells would be expected to contain the DNA, it is not clear as to how the DNA can be considered to be "prostate cancer specific." It is also not clear if this recitation is only "lung cancer specific" in humans or whether it can be specific in other animals as well. Furthermore, the specification does not specifically define this recitation.

B) Claims 1-5, 7-9, 15 and 18-28 are indefinite over “detectably expressed specifically in lung cancer tissue” because it is not clear as to what is meant or encompassed by this recitation. For example, it is not clear as to whether this means the claimed nucleic acid molecules were only expressed in lung cancer tissue samples and not expressed in normal lung tissue samples, or the claimed nucleic acid molecules were highly expressed in lung cancer tissue samples, as compared to the expression in normal lung tissue samples, etc. Furthermore, the specification does not define what is meant by “detectably expressed specifically in lung cancer tissue.”

C) Claims 24-28 are indefinite over “wherein sequence identity is over at least 250 nucleotides” because it is not clear as to what “sequence identity” is being referred to. If Applicants intend these claims to be dependent from 1(d), which does specify, “sequence identity,” it is suggested that Applicants amend the claims to clearly reflect this.

***Claim Rejections - 35 USC § 101***

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-5, 7-9, 15 and 18-28 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility, or a well-established utility.

The pending claims have been reviewed in light of the Utility Examination Guidelines in the Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday, January 5, 2001, as well as the MPEP and existing law.

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I. *The specification does not assert a substantial utility because the utilities asserted by Applicants requires or constitutes carrying out further research to identify or reasonably confirm a “real world” use.*

Applicants assert the claimed nucleic acid can be used in methods “for identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung.” (see page 7, lines 22-24).

The specification teaches a data mining experiment for identifying nucleic acids (see pages 116-120). Specifically, the specification teaches SEQ ID NO: 51 was identified by data mining of sequences in the Incyte Genomics LIFESEQ database using CLASP software (see pages 116-118). SEQ ID NO: 51 was procured from, and thereby known by Incyte Genomics Inc. (see page 116). Applicants allege that SEQ ID NO: 51 is considered to have a “CLASP 2CLASP1” profile (page 118, line 45), wherein:

To qualify as a CLASP 2 candidate, a gene must exhibit detectable expression in tumor tissues and undetectable expression in libraries from normal individuals and libraries from normal tissue obtained from diseased patients. In addition, such a gene must also exhibit further specificity for the tumor tissues of interest.

To qualify as a CLASP 1 candidate, a gene must exhibit statistically significant expression in the tissue of interest compared to all other tissues. Only if the gene exhibits such differential expression with a 90% of confidence level is it selected as a CLASP 1 candidate.

(see page 117, lines 12-16 and lines 22-26).

The specification is silent with respect to any potential nucleic acids that fall within Claim 1(c) or (d) or Claims 20-28 (i.e., there is not CLASP profile for these nucleic acids).

Other than Applicants characterization that SEQ ID NO: 51 has a “CLASP2CLASP1” profile, there is no data or experimental analysis of SEQ ID NO: 51 or the other claimed nucleic

acids. The specification does not teach what tissues were used, whether diseased and normal samples were expressed and then compared against one another, how many patients these results stem from, relative expression levels of tissues, and furthermore, it is not clear as to what was the source of the nucleic acids (e.g., cell lines or primary tumor cells).

MPEP § 2107.01 states:

A “substantial utility” defines a “real world” use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a “real world” context of use are not substantial utilities... An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a “real world” context of use in identifying potential candidates for preventive measures or further monitoring.

In the instant case, further research to identify or reasonably confirm a “real world” context of use would be required. For example, in order for a nucleic acid to be useful for detection, diagnosis and/or treatment of a disease, there must be a well established or disclosed correlation or relationship between the claimed nucleic acid and a disease or disorder. The presence of a nucleic acid in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed nucleic acid and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed nucleic acid to be used in a diagnostic manner. Many nucleic acids are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed nucleic acid is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed nucleic acid as a diagnostic for a disease. However, in the absence of any disclosed relationship between the

claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. “Congress intended that no patent be granted on a chemical compound whose sole ‘utility’ consists of its potential role as an object of use-testing.” *Brenner v. Manson*, 148 USPQ 6174 (US SupCt 1966).

Specifically, in the instant case, the specification does not provide any assay or evidence that clearly demonstrates a correlation between SEQ ID NO: 51 (or nucleic acids encompassed by Claim 1, (c) or (d) or Claims 20-28) and methods for identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung. The specification does not teach any assay or expression analysis that indicates the relationship between SEQ ID NO: 51 (or nucleic acids encompassed by Claim 1, (c) or (d) or Claims 20-28) and lung cancer. At best, Applicants have proposed a starting point for further research in order to determine whether SEQ ID NO: 51 is correlated with lung cancer. Accordingly, the disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. 101.

II. *The specification is not supported by a well-established utility because one of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics on the invention.*

MPEP 2107 states:

An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.”

Applicants have provided little to no evidence of the characteristics of the claimed nucleic acids, the asserted utility is not substantial, and based on Applicants assertion that the

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claimed nucleic acid is new (see page 1, lines 9-10), it is not apparent as to how “a person of ordinary skill in the art would immediately appreciate why the invention is useful”. This is evidenced by the fact that further research would need to be carried out by the skilled artisan even given Applicants’ claimed nucleic acids (see above). For these reasons, the specification is not supported by a well-established utility.

Accordingly, the claimed invention lacks a substantial and well-established utility.

***Claim Rejections - 35 USC § 112***

6. Claims 1-5, 7-9, 15 and 18-28 also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, in addition to the reasons above, the specification is further not enabling because the specification does not establish that in the general population SEQ ID NO: 51 is overexpressed in lung tumor versus other tumor cells or versus normal cells.

MPEP 2164.01 states:

Even though the statute does not use the term ‘undue experimentation,’ it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The *Wands* court outlined several factors to be considered in determining whether a disclosure would require undue experimentation. These factors include, but are not limited to:

- (1) the quantity of experimentation necessary, (2) the amount of direction or

guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” *Id.* at 1404.

In the instant case, the specification does not enable one of skill in the art to make and use the claimed invention for the following reasons:

**(1) *Nature of the Invention & Breadth of the Claims***

The claims are drawn to isolated nucleic acid molecules comprising a nucleic acid sequence encoding SEQ ID NO: 174, a nucleic acid of SEQ ID NO: 51, nucleic acid molecules that selectively hybridize under stringent conditions to a nucleic acid that encodes SEQ ID NO: 174 or a nucleic acid of SEQ ID NO: 51, and nucleic acids having at least 96% sequence identity over at least 200 nucleotides of SEQ ID NO: 174 or a nucleic acid of SEQ ID NO: 51.

Thus, the claims are drawn to a large genus of possible nucleic acids, including sequences from other species, mutated sequences, and allelic variants having different functional activities than that of the nucleic acids of SEQ ID NO: 51, and nucleic acids encoding the polypeptide of SEQ ID NO: 174.

**(2) *Relative Skill of those in the Art, State of the Prior Art, Amount of Direction or Guidance Presented & Presence or Absence of Working Examples***

The specification teaches SEQ ID NO: 51 was procured from, and thereby known by Incyte Genomics Inc. (see page 116). However, the specification does not provide any working examples of using the claimed nucleic acids for identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung. Additionally, the specification does not provide any evidence the claimed nucleic acids can be in fact be used in

identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung.

Furthermore, the specification does not teach several elements that would be necessary to enable the skilled artisan to use the nucleic acids of the invention. First, it is not clear as to what the source of the library is (e.g., primary tumor cells versus a cell line) from which the claimed nucleic acids were obtained from. This is an important inquiry, since gene expression in primary tumor cells is often distinct from that which occurs in cell lines (see Dermer et al.

Bio/Technology (1994) 12: 320). Assuming Applicants procured the claimed nucleic acids from a primary tumor, the specification does not teach how many samples are present in the library. If Applicants derived expression results from a library containing only one sample, any expression data would not be applicable to the general population. That is, data from one individual is not representative of data that will or may occur in other diseased or normal patients. Thus, even assuming the specification teaches the claimed nucleic acids are overexpressed in lung tumor cells obtained from a single source, the specification has not established that in the general population that the claimed nucleic acids are overexpressed in lung tumor versus normal cells. Additionally, the specification does not teach a comparative readout of expression data among lung tissue (if tested) versus expression of the claimed nucleic acids in other tissues. There is no data showing overexpression in lung tumor cells versus other tumor cell types (e.g., from ovary, breast, etc.) or normal tissue cells (e.g., from lung, ovary, breast, etc.). Furthermore, the specification does not teach what sequences were being compared in the CLASP analysis, what tissues were involved, what types of individuals were screened, and what activity or function the polypeptide of SEQ ID NO: 174 has.

With respect to Claim 1(c) and (d) and Claims 20-28, the claims are drawn to a plurality of possible nucleotide sequence variants of SEQ ID NO: 51, wherein the specification does not provide any guidance as to how to alter nucleic acid sequences falling within Claim 1(c) and (d) and Claims 20-28, nor does it teach how to use said sequences. Specifically, the specification is silent as to any nucleotide sequences falling within Claim 1(c) and (d) and Claims 20-28. Furthermore, the specification does not teach the critical domains, if any, of the polypeptide encoded by the nucleotide sequences falling within Claim 1(c) and (d) and Claims 20-28.

Accordingly, the relative skill in the art is high, there are no working examples provided for using the claimed nucleic acids, and the specification has provided little to no guidance for using the claimed nucleic acids.

**(3) *Quantity of Experimentation Necessary & the Unpredictability of the Art***

Case law has established that “(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *In re Wright* 990 F.2d 1557, 1561. In *In re Fisher*, 517 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that “(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art”. The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art.

In the instant case, the specification, nor the prior art teach an association/and or correlation for SEQ ID NO: 51 (or nucleic acids encompassed by Claim 1(c) or (d) or Claims 20-28), and therefore, the skilled artisan would not know how to use the claimed nucleic acids. Any potential results that the skilled artisan would arrive at would be unpredictable given the lack of

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guidance in the specification and the prior art (see above). For example, the specification teaches that the tumor of interest (i.e., lung tumor library) was compared to normal libraries for all tissues (see page 117). However, it is not clear as to whether all the normal tissues were combined, since there is no expression data for any tissues. It is especially noted that there is no data of normal lung expression. However, assuming that SEQ ID NO: 51 is overexpressed, and the specification only teaches the expression of combined normal tissues (versus normal lung tissue expression), the skilled artisan would not know how to practice the invention because it is not clear as to what level of expression is associated with cancer. Additionally, given the lack of guidance in the specification or the prior art, as to how to alter the claimed nucleotide molecules and retain the activity of SEQ ID NO: 174, the making and using of the nucleic acid molecules encompassed by the claimed invention would also be unpredictable. Finally, the suitability of cell lines, as general models for primary tumors are also unpredictable. For example, Dermer (cited above) teaches:

[w]hen a normal or malignant body cell survives a crisis period and adapts to immortal life in culture, it takes an evolutionary type step that enables the new cell line to thrive in its artificial environment... Yet normal or malignant cells *in vivo* are not like that. This means that cell lines are really a new life form on Earth, neither human nor animal. Evidence of the contradictions between life on the bottom of the lab dish and in the body has been in the scientific literature for more than 30 years, evidence that has been systematically ignored by the cancer establishment.

(1<sup>st</sup> column, page 320).

Therefore, if the nucleic acids in Example 1 were procured from cell lines, then extrapolating expression data from SEQ ID NO: 51 for identifying, diagnosing, monitoring, staging, imaging and treating lung cancer and non-cancerous disease states in lung would be highly unpredictable.

In order to carry out making and using of the claimed nucleic acids, the experimentation required by the skilled artisan would be considered undue. First, the skilled artisan would have to experiment by altering any of the plurality of possible sequences encompassed by the claims to determine what sequences can be altered, and how they can be altered, and still retain the function of SEQ ID NO: 174. Additionally, once the sequences were obtained, the skilled artisan would have to carry out expression analysis studies on many samples from different tissues from both normal and diseased test subjects (including normal and malignant lung tissues from cell culture and patients' samples, as well as, in cells from unrelated tissues). Following this experimentation, the skilled artisan would have to determine whether the sequences are specific for a disease state. Significance of any increased expression levels needs to be established; as there are usually variations in tissues obtained from different individuals, therefore studies involving statistically significant numbers of patients would also need to be performed. Such experimentation requires a large amount of trial and error analysis, with little to no starting point, absent any teaching in the specification (see above), wherein the results of such analysis are unpredictable, and is therefore considered undue.

In essence, the experimentation that one skilled in the art would be required to perform is in fact the proposed novelty of the invention. However, “(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement”. (*Genetech Inc. v Novo Nordisk* 51 USPQ2d 1001).

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

### **Applicants Arguments**

Applicants argue the identification of “SEQ ID NO: 51 as having detectable expression specific for lung cancer tissue constitutes a pharmacological activity relevant to the asserted use as a diagnostic for lung cancer, thus satisfying the utility requirement.” See page 21 of Applicants response. Applicants also argue the specification teaches detailed teachings of nucleic acid molecules meeting the limitations of Claim 1(c) and (d) on pages 31-40, and that “MPEP § 2107.03 and the courts are quite clear, evidence of structural similarity to a compound known to have a particular therapeutic or pharmacological utility is routinely supportive of an assertion of therapeutic utility for the structurally similar compound.” See page 21 of Applicants response. Applicants also reiterate some of the issues raised in the rejection, such as “what tissues were used,” “how many patients these results stem from,” and “relative expression levels in tissues and the source of the nucleic acids is (e.g., cell culture of tumor).” See page 19 of Applicants response.

### **Response to Applicants Arguments**

Applicants’ arguments have been considered, but are not persuasive for the following reasons. First, it is not clear as to what is meant or encompassed by “detectably expressed specifically in lung cancer tissue,” and therefore, it is not clear what expression levels were actually obtained, if any, in samples from lung cancer tissue libraries or normal lung tissue libraries. (See 112, 2<sup>nd</sup> paragraph above) Next, Applicants did not show either that the nucleic acids encompassed by the claims are expressed only in lung cancer tissue or that they have any pharmacological activity. Applicants have not provided any comparative data for the level of

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expression of the claimed nucleic acids in cancerous vs. normal tissue, which is critical to the utility of claimed nucleic acids as being indicative of tumorigenesis. In addition, despite Applicants' assertions, pages 31-40 do not provide any specific nucleic acid sequences (or variants) of the nucleic acids encompassed by Claim 1(c) or (d) or Claims 20-28. Furthermore, even assuming Applicants did provide these structural descriptions, SEQ ID NO: 51 does not have a "particular therapeutic or pharmacological utility," and therefore, the nucleic acids of Claims 1(c) and (d) and Claims 20-28 do not meet the utility requirements. Finally, while Applicants reiterate issues raised in the rejection (e.g., "what tissues were used," "how many patients these results stem from," and "relative expression levels in tissues and the source of the nucleic acids is (e.g., cell culture of tumor)," Applicants do not provide explanations to these issues. Accordingly, the rejection is maintained.

***Written Description***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 7-9, 15 and 20-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The Claims are directed to nucleic acids comprising a nucleic acid sequence encoding SEQ ID NO: 174, a nucleic acid of SEQ ID NO: 51, nucleic acid molecules that selectively

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hybridize under stringent conditions to a nucleic acid that encodes SEQ ID NO: 174 or a nucleic acid of SEQ ID NO: 51, nucleic acids having at least 96% sequence identity over at least 200 nucleotides of the nucleic acid sequence encoding SEQ ID NO: 174 or a nucleic acid of SEQ ID NO: 51, nucleic acids wherein sequence identity is over at least 250 nucleotides of the nucleic acid molecule of that encodes SEQ ID NO: 174 or a nucleic acid of SEQ ID NO: 51, wherein said nucleic acid molecules are detectably expressed in lung cancer tissue. These nucleic acids are inclusive of sequences from other species, mutated sequences, allelic variants, full-length genes, genomic DNA, etc., all which have different functions than that of the nucleic acid encoding SEQ ID NO: 174. Accordingly, the claims include a large genus of nucleic acids encoding polypeptides, having unique functional activities, whereas applicants only disclose one member of the genus (i.e., SEQ ID NO: 51).

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only one member (SEQ ID NO: 51) has been defined by its structure. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., restriction map, chromosomal map position, biological activity of an encoded protein, promoters, enhancers, 5' or 3' untranslated regions, etc.). In the instant case, no such identifying characteristics have been provided for any of the nucleic acids. For example, the specification does not reasonably convey to one skilled in the art that Applicants were in possession of the claimed invention, because the specification does not describe the specific structures (e.g., promoters, enhancers, 5' or 3' untranslated regions), which are found in genomic DNA (i.e., which is encompassed by the

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instant claims), or any of the other types of nucleic acid molecules encompassed by the broadly claimed invention. More specifically, the specification only describes SEQ ID NO: 51 (which encodes SEQ ID NO: 174), but does not describe the other types of nucleic acid molecules encompassed by the claims.

In *The Reagents of the University of California v. Eli Lilly and Co.*, (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA... ‘requires a precise definition, such as by structure, formula, chemical name, or physical properties,’ not a mere wish or plan for obtaining the claimed chemical invention”. In the instant case, the claims are drawn to generic statements, which define a genus of nucleic acids by only their alleged functional activity; however, the specification does not provide an adequate written description of this genus.

*Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed (See page 1117).” (emphasis added)

While at the time filing Applicants were in possession of SEQ ID NO: 51, the specification does not support the broadly claimed genus. Accordingly, the claimed invention lacks an adequate written description.

Applicant's attention is also drawn to the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1<sup>st</sup> Paragraph, Written Description Requirement" (published in Federal Register/Vol. 66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111).

### **Applicants Arguments**

Applicants argue amended Claim 1, which was amended to "clarify that the nucleic acid molecule is lung cancer specific and detectably expressed in lung cancer tissue," and therefore, "the nucleic acid molecules have a similar function." See pages 22-23 of Applicants' response. Applicants also argue pages 13-16 and Example 1 teaches methods for ascertaining sequences that meet the structural and functional limitations of the instant amended claims. See page 23 of Applicants' response. Furthermore Applicants argue "upon discovery of the instant claimed nucleic acid sequence of SEQ ID NO: 51 and its lung tissue specificity and lung cancer tissue specificity, Applicants were clearly in possession of additional nucleic acid sequences identified in accordance with routine procedures based upon these reference sequences." See pages 23-24 of Applicants' response.

### **Response to Applicants Arguments**

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, it is not clear what is meant by "lung cancer specific" and "detectably expressed in lung cancer tissue," and therefore, it is not clear what functional limitation this adds to the Claim 1 (see 112, 2<sup>nd</sup> paragraph rejection above). Next, while pages 13-16 and Example 1

teaches general concepts relating to sequence identity, sequence similarity and hybridization parameters, these passages do not demonstrate that Applicants were in *possession* of the genus of nucleic acids encompassed by the claims. Furthermore, the assertion that a skilled artisan performs some methods routinely does not mean that Applicants were in possession of the claimed nucleic acids. Except for the description of SEQ ID NO: 51, Applicants have not provided an adequate written description to support the broadly claimed genus of nucleic acids. Finally, it is not clear how the disclosure of SEQ ID NO: 51 and its alleged lung tissue specificity and lung cancer tissue specificity, demonstrates that Applicants were “clearly” in possession of additional nucleic acids. There is no evidence in the record to support Applicants assertions that given the disclosure of SEQ ID NO: 51, Applicants were “clearly” in possession of additional nucleic acids encompassed by the claims. Accordingly, the rejection is maintained.

***New Matter***

9. Claims 1-5, 7-9, 15 and 18-25 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1(d) recites, “a nucleic acid molecule having at least 96% sequence identity over at least 200 nucleotides.” However, the specification does not provide support for this specific sequence identity “at least 96%” for this specific stretch of nucleotides “at least 200 nucleotides.” Pages 32-33 discuss varying sequence identities and nucleic acid fragments;

however, these pages do not specifically support “a nucleic acid molecule having at least 96% sequence identity over at least 200 nucleotides.” According, the recitation of Claim 1(d) constitutes new matter.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-5, 7-9, and 18-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Furness et al. (USPN 6,673,549).

Furness teaches SEQ ID NO: 962, which is 100% identical to instant SEQ ID NO: 51 (see Pending Patents search result #1).

With respect to Claims 2-3, Furness teaches the nucleic acid is cDNA or genomic DNA (see abstract and cols. 8-9).

With respect to Claims 4-5, Furness teaches the nucleic acid is a mammalian (e.g., human) nucleic acid molecule (see col. 24, for example).

With respect to Claims 7-9, Furness teaches vectors, host cells and methods of producing a polypeptide (see cols. 5-6)

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (11746), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Furness et al. (USPN 6,673,549), as applied to Claims 1-5, 7-9, 18-28, in view of the Stratagene Catalog (1988).

Furness teaches a means for determining the presence of the claimed nucleic acids (see cols. 15-16, for example). Furness does not teach packaging said means into a kit.

However, reagent kits for performing DNA assays were conventional in the field of molecular biology at the time the invention was made. In particular, the Stratagene Catalog discloses that kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatibility of the reagents to be used in the assay. Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have packaged a means for determining the presence of the claimed nucleic acids in a kit for the expected benefits of convenience and cost-effectiveness for practitioners of the art.

#### MAINTAINED REJECTIONS

##### *Claim Rejections - 35 USC § 102*

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (f) he did not himself invent the subject matter sought to be patented.

17. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by the Incyte Genomics LIFESEQ™ Database.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc.

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(via the Incyte Genomics LIFESEQ database) at the time the invention was made. Accordingly, the nucleic acids of the present invention were known and used in the art prior to the filing of the instant application. The nucleic acid appears to be cDNA from human samples (claims 2 and 4-5).

18. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc. (via the Incyte Genomics LIFESEQ database) at the time the invention was made. Accordingly, the nucleic acids of the present invention were in public use and on sale in this country prior to the filing of the instant application. The nucleic acid appears to be cDNA from human samples (claims 2 and 4-5).

19. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The specification at page 116 states that the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc. (via the Incyte Genomics LIFESEQ database) at the time the invention was made. Accordingly, it appears that Applicant did not invent the claimed subject matter. The nucleic acid appears to be cDNA from human samples (claims 2 and 4-5).

#### **Applicants Arguments (Incyte Genomics LIFESEQ™ Database, 102 Rejections)**

Applicants argue the specification does not state that the nucleic acids were procured from or known by Incyte Genomics Inc. See Applicants' response on page 25. Applicants argue

they utilized their own set of algorithms referred to as CLASP™ to systematically “interrogate and analyze gene expression data in the LIFESEQ Gold database”. See Applicants’ response on page 25. Furthermore, Applicants argue that but for their proprietary CLASP™ algorithms, one of skill in the art would not know the claimed nucleic acids are “lung cancer specific”. See Applicants’ response on page 26. Applicants also argue they have amended the claims to recite “lung cancer specific” to distinguish the present invention from expression data in the LIFESEQ Gold database. See Applicants’ response on page 26.

### **Response to Applicants Arguments**

Applicants’ arguments have been considered, but are not persuasive for the following reasons. As taught in the specification, and again asserted in Applicants arguments, the claimed nucleic acids were contained in the LIFESEQ Gold Database and available from Incyte Genomics Inc. Despite using their own algorithms, Applicants state they “interrogate[d] and analyze[d] gene expression data *in* the LIFESEQ Gold database”. That is, Applicants algorithms analyzed data (nucleic acid sequence and expression data) *from* Incyte Genomics Inc. and determined what nucleic acids sequences were “lung cancer specific”. Thus, Applicants procured the sequence information, e.g., SEQ ID NO: 51 from Incyte Genomics Inc., and therefore, Applicants did not invent SEQ ID NO: 51. Applicants seek to distinguish the data obtained from Incyte and the claimed nucleic acids by having amended the claims to recite “lung cancer specific”. However, the claimed nucleic acids are still the same product, having the same structure, as the nucleic acid sequence information obtained from Incyte. The claims are drawn to products, not to methods of using the products, and therefore, absent any evidence of a structural distinction between the claimed nucleic acids and that of the nucleic acid sequences

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from the LIFESEQ Gold database, the claimed invention is structurally the same as the sequences in the LIFESEQ Gold database, and are therefore anticipated by LIFESEQ Gold database. It is also noted, it is not clear what is meant or encompassed by “lung cancer specific” (see 112, 2<sup>nd</sup> paragraph rejection above). Accordingly, the rejection is maintained.

20. Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Birren et al. (GenEmbl Accession No. AC032035).

Birren teaches a nucleic acid comprising a nucleic acid molecule that selectively hybridizes under stringent conditions to SEQ ID NO: 51 (see GenEmbl Accession No. AC032035, see sequence search result #2). It is noted that the claims encompass nucleic acids comprising “a” nucleic acid of SEQ ID NO: 51, and therefore, GenEmbl Accession No. AC032035 is considered to anticipate the claimed invention. In other words, because the claims recite “a” nucleic acid, the claims include portions (i.e., partial sequences) of SEQ ID NO: 51, wherein the portions may be of any length. Furthermore, because the claims recite, “comprising”, the claims include nucleic acids, which contain this portion and an unlimited number of flanking nucleotides.

With respect to Claims 2 and 4-5, Birren teaches the nucleic acid is from a cDNA clone and that the nucleic acid is a mammalian (e.g., human) nucleic acid molecule (see sequence search result #2).

### **Applicants Arguments**

Applicants argue the amendments to Claim 1 obviate the rejections of Birren. Applicants specifically argue “a nucleic acid molecule of SEQ ID NO: 51” has been removed.

### **Response to Applicants Arguments**

Applicants' arguments have been considered, but are not persuasive. The nucleic acid taught by Birren will selectively hybridizes under stringent conditions to a SEQ ID NO: 51, and therefore, the teachings of Birren anticipate the claimed invention. It is also noted, "a nucleic acid molecule of SEQ ID NO: 51" still appears in Claim 1. Accordingly, the rejection is maintained.

21. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Mullis et al. (USPN 4,800,159).

Mullis et al. teach a kit comprising a means for determining the presence of the nucleic acid molecule of claim 1 in a sample of a patient (e.g., agent for polymerization, nucleoside triphosphates, means for detecting hybrids of a probe and a sequence, etc.) (see col. 3, for example).

### **Applicants Arguments**

Applicants argue the kit of Mullis "in no way teaches a means of detection of" the specific nucleic acids of Claim 1.

### **Response to Applicants Arguments**

Applicants' argument has been considered, but is not persuasive. First, the claimed kit does not contain any specific components or reagents that are considered to be "a means for determining the presence [of] the nucleic acid molecules of Claim 1," which distinguishes the claimed kit from the kit of Mullis. Furthermore, Mullis teaches a kit comprising a means for detecting a nucleic acid sequence (see col. 3, for example). Absent a specific nucleic acid probe of a particular sequence, for example, Mullis' kit comprising a means for detecting a nucleic acid

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sequence anticipates “a means for determining the presence [of] the nucleic acid molecules of Claim 1.” Accordingly, the rejection is maintained.

***Claim Rejections - 35 USC § 103***

22. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Incyte Genomics' LIFESEQ Database, as applied to claims 1-2 and 4-5 above, and further in view of Prendergast (USPN 5,958,753).

As discussed in the specification (pg. 116) the nucleic acids of the present invention (including SEQ ID NO: 51) were procured from, and thereby known by Incyte Genomics Inc. (via the Incyte Genomics LIFESEQ database) at the time the invention was made. The cited prior art does not teach expressing the nucleic acids using an expression system.

However, Prendergast teaches operably linking a polynucleotide into an expression vector, transforming a host cell with the resulting recombinant vectors and expressing the polypeptides encoded by the polynucleotide using the transformed host cells (see cols. 5-6, for example).

Accordingly, in view of the teachings of Prendergast, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have linked the polynucleotides of the LIFESEQ Database into expression vectors, to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides. One of ordinary skill in the art would have been motivated to do so in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides, which would have allowed for the further characterization of the functional properties of the isolated polynucleotides and the products encoded by the isolated polynucleotides.

**Applicants Arguments**

Applicants argue that only given the teaching of the instant specification would one of skill in the art be motivated to link the claimed nucleic acid molecules into vectors and to have expressed said vectors into host cells. See Applicants' response on page 31. Applicants also assert the claimed invention, as amended to include "lung cancer specific", distinguishes the instant invention over the prior art. See Applicants' response on page 31.

**Response to Applicants Arguments**

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, it is not clear what is meant or encompassed by "lung cancer specific" (see 112, 2<sup>nd</sup> paragraph rejection above). Next, with respect to Applicants assertions the claimed products are different than that of the LIFESEQ Gold Database, see the above discussion under "Response to Applicants Arguments" following the 102 rejections over the LIFESEQ Gold Database. Furthermore, even assuming one of skill in the art would not have been motivated to have linked the claimed nucleic acids in a vector and subsequently have expressed said vector in a host cell for lung cancer specific expression, one of skill in the art would have been motivated to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides, which would have allowed for the further characterization of the functional properties of the isolated polynucleotides and the products encoded by the isolated polynucleotides. Accordingly, the rejection is maintained.

23. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birren et al. (GenEmbl Accession No. AC032035), as applied to claims 1-2 and 4-5 above, and further in view of Prendergast (USPN 5,958,753).

The teachings of Birren are presented above. Specifically, Birren teaches GenEmbl Accession No. AC032035 which has a best local similarity of 95.1% identity to Applicant's SEQ ID NO: 51 (see sequence search result #2), and therefore, encompasses the claimed nucleic acid. Birren does not teach expressing the nucleic acids using an expression system.

However, Prendergast teaches operably linking a polynucleotide into an expression vector, transforming a host cell with the resulting recombinant vectors and expressing the polypeptides encoded by the polynucleotide using the transformed host cells (see cols. 5-6, for example).

Accordingly, in view of the teachings of Prendergast, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have linked the polynucleotides of Birren into expression vectors, to have transformed host cells with the resulting vectors and to have used the transformed cells to express polypeptides. One of ordinary skill in the art would have been motivated to do so in order to have provided an effective means for synthesizing polypeptides encoded by the isolated polynucleotides, which would have allowed for the further characterization of the functional properties of the isolated polynucleotides and the products encoded by the isolated polynucleotides.

### **Applicants Arguments**

Applicants argue Birren does not teach the nucleic acid molecules of Claim 1, and Prendergast fails to remedy the alleged deficiencies of Birren. See response on page 32.

### **Response to Applicants Arguments**

Applicants argument has been considered, but is not persuasive, since Birren does teach a nucleic acid molecule encompassed within Claim 1, and Prendergast teaches the requisite motivation to have linked the nucleic acid of Birren into an expression vector, transforming a host cell with the resulting recombinant vector and expressing the polypeptides encoded by the nucleic acid using the transformed host cell. Accordingly, the rejection is maintained.

### ***Conclusion***

24. No claims are allowable.
25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).  
Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

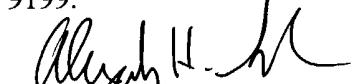
If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (571) 272-0747. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

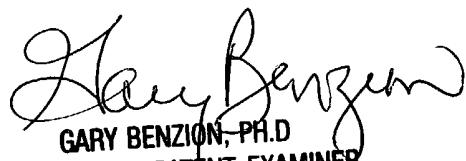
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Alexander H. Spiegler

August 3, 2004

  
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